

### **REMARKS/ARGUMENTS**

Claim 1 has been amended to specify that the Hcy and Mesna are removed from the plasma during dialysis. Basis for this amendment is found, for example, on page 7, lines 18-20, and on page 19, lines 15-17, of the application as filed.

Claims 1-5 and 7-15 are pending in the present application.

The Official Action dated December 22, 2008, has been carefully considered. It is believed that the amended claims submitted herewith and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

The Applicants acknowledge and appreciate the Examiner's removal of his comments regarding the election and restriction, the objection to claim 4 and the rejection of claim 14 under 35 USC 112.

#### **35 UCS § 103(a)**

The Examiner has maintained the rejection of claims 1, 3-5 and 7-14 under 35 USC § 103(a) as being obvious over Pendyala, et al. Clinical Cancer Research, 2000, 6(4):1314-1321 (herein after "Pendyala") and Cohen, Molecular and Cellular Biochemistry, 2003, 244(1-2):31-36 (herein after "Cohen"), in view of Wilcox, WO 01/30352 A1, 2001 (hereinafter "Wilcox").

The Examiner has acknowledged that Figure 13 of the present application shows that Mesna is removed from the blood stream into the dialysate during dialysis. However, the Examiner did not consider the Applicants' discussion of the two references (i.e. Friedman et al. and Ventura et al.) as these articles were not present in the patent office record and therefore could not be used to establish the position that these results would

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have been unexpected based on the knowledge in the art at the time the present application was filed.

In view of the above, the Applicants have resubmitted, herewith, the Information Disclosure Statement (IDS) that was filed on August 15, 2006, as well as the documents cited in that statement. These documents include Friedman et al. (#15) and Ventura et al. (#16). Also included in the IDS submitted herewith are the documents Kuhlmann, M.K. Hemodialysis International, 2006, 10:338-345, and Sengupta et al. Journal of Biological Chemistry, 2001, 276:30111-30117, referred to in the previous response.

In view of the arguments presented in the previous response and the placement of Friedman et al. and Ventura et al. on the record, the Applicants submit that they have now provided support for the surprising and unexpected finding described in the present application that Mesna was able to decrease post-dialysis t-Hcy while, it itself is also removed from the plasma during dialysis, in patients with ESRD.

The Applicants also direct the Examiner to the information provided in the publication entitled "2002 Dialysis of Drugs" by Curtis A. Johnson and William D. Simmons, Nephrology Pharmacy Associates, Inc. USA 2002 (included in the UDS submitted herewith). In this publication, it is clearly indicated that, prior to the present application, the ability of mesna to be removed by dialysis was undetermined (see page 37). Further, the authors were not able to predict whether or not mesna could be removed by dialysis using "information extrapolated from studies using conventional dialysis techniques". This combined with the knowledge that mesna possesses certain undesirable side effects, which would be more serious in patients with ESRD, further supports the unpredictability and non-obviousness of the presently claimed invention.

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The Examiner has further noted that the expectation for liberation of mesna is not a component of the claims. In view of this, the Applicants have amended claim 1 to clarify that dialysis removes Hcy and Mesna from the plasma.

In view of the above amendments and arguments the Applicants request that the Examiner's rejection of claims 1, 3-5 and 7-14 under 35 USC 103(a) be withdrawn.

In view of the foregoing, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, he is kindly requested to contact Patricia Folkins by telephone at 416-957-1683 at his convenience.

The Commissioner is hereby authorized to charge any deficiency in fees or credit any overpayment to our Deposit Account No. 02-2095.

Respectfully submitted,

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